## REMARKS

### I. Status of the Claims

Claim 15 has been amended to recite "wherein said acrylic polymer is soluble in the stomach" to indicate the types of acrylic polymers which are contemplated in the instant invention – namely acrylic polymers soluble in stomach acid and not acrylic polymers insoluble in the stomach but soluble in the upper gastrointestinal tract. Support for the amendment may be found throughout the specification, particularly at page 5, line 24 and page 8, line 23. New claim 42 has been added and finds support in the application as filed at page 8, line 12. No prohibited new matter is believed to have been added. Claims 15-42 are now pending. Claims 15-28 and 40-42 are under examination, and claims 29-39 are withdrawn.

### II. Rejections under 35 U.S.C. §112, first paragraph and second paragraphs

The Examiner did not reiterate the rejection of claims 15-28 under 35 U.S.C. §112, first paragraph and claim 23 under 35 U.S.C. §112, second paragraph in the Office Action dated 11/17/2009 and as such Applicants understand that these rejections have been withdrawn.

### IV. Rejection of Claims 15-17, 19-21, 23-24 and 26-28 under 35 U.S.C. §102(e) as Anticipated by *Percel* (US 6,451,345)

Claims 15-17, 19-21, 23-24 and 26-28 stand rejected under 35 U.S.C. §102(e) as being allegedly anticipated by *Percel* (US 6,451,345). Applicants strongly disagree.

The presently claimed invention is directed to pharmaceutical microcapsules with enhanced taste-masking and high dissolution rate in the stomach. The invention as presently claimed encompasses microcapsules which comprise drug microparticles surrounded by a first layer consisting essentially of ethylcellulose which itself is surrounded by a second layer which comprises an acrylic polymer that is soluble in the stomach. A disclosed example of an acrylic polymer which is soluble in the stomach is Eudragit E, an amine functional which is "practically

insoluble in … water", but is completely soluble in 1N HCl.[1]

In contradistinction, *Percel* discloses a taste-masked rapid release coating system comprising granules that "rapidly release (as a burst) at pH's of the upper intestinal tract" (abstract), and "the microencapsulated crystals are provided with an enteric polymer coat" [2](col. 3, ll. 28-30). Applicants note that it is well known that the pH of the upper intestinal tract is essentially neutral[3], and that enteric polymers are by definition *insoluble* at the pH of the stomach, but soluble at the higher pH levels of the small intestine.[4] In other words, the enteric polymers of *Percel* are not soluble in the stomach, but are soluble at the essentially neutral pH levels of the small intestine, whereas the acrylic polymers of the claimed invention have essentially the *opposite* solubility characteristics – soluble in the stomach but insoluble at neutral pH.

Since *Percel* does not disclose "a second layer disposed over said first layer, comprising an acrylic polymer, wherein said acrylic polymer is soluble in the stomach", Percel can not anticipate the instantly claimed invention.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

## IV. Rejection of Claims 15-17, 19-20, 23-28 under 35 U.S.C. §102(b) as being allegedly anticipated by *Holt* (WO 00/30617)

Claims 15-17, 19-20, and 23-28 stand rejected under 35 U.S.C. §102(b) as being allegedly anticipated by *Holt* (WO 00/30617). Applicants strongly disagree.

The presently claimed invention is described above. The Examiner alleges that *Holt* teaches

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[1] Specification sheet for Eudragit E 100, Degussa.
[2] col. 3, ll. 28-30
[3] *See, e.g.,* "Digestion" article, Wikipedia, in which the secretion of bile and pancreatic bicarbonate into the duodenum (first section of the small intestine) neutralizes stomach acid, "creating a neutral environment."
[4] *See, e.g.,* Remington, The Science and Practice of Pharmacy, 21st Ed., pp. 932-933.

"a taste-masked rapid release coating system comprised of a drug core …, a spacing layer that includes ethyl cellulose and a taste-masking layer that includes Eudragit polymers.[5]

Applicants note that claim 15 recites that the first layer disposed over the microparticles *consists essentially of* ethyleellulose. The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention.[6] *Holt* discloses that the materials useful for the "spacing layer" include ethyl cellulose, methyl cellulose, hydroxy propyl cellulose, hydroxy propyl methyl cellulose, polyalkylene glycols, polyalkylene oxides, sugars and sugar alcohols, waxes, shellacs, acrylics, etc. and mixtures thereof.[7] The only guidance given beyond this list is in Examples 1, 2, 3, and 4 – all of which use ethyl cellulose combined with polyvinylpyrrolidone (PVP) or hydroxypropyl methyl cellulose (HPMC). Ethylcellulose is practically insoluble in water, whereas PVP and HPMC are well known in the pharmaceutical arts as water-soluble polymers. As such, both PVP and HPMC would reasonably materially affect the solubility characteristics of a water insoluble polymer such as ethyl cellulose when combined therewith. Therefore, the transition phrase *consisting essentially of* recited in claim 15 excludes the mixtures of ethyl cellulose/PVP and ethyl cellulose/HPMC disclosed in *Holt* and, thus, *Holt* does not anticipate claim 15, nor the claims dependant thereon.

Accordingly, Applicants respectfully request the reconsideration and withdrawal of this rejection.

## V. Rejection of Claims 15-24 and 26-28 under 35 U.S.C. §103(a) as being allegedly unpatentable over *Percel.*

Claims 15-24 and 26-28 stand rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over *Percel*. Applicants disagree.

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[5] Office Action dated 2/27/2009
[6] MPEP 2111.03 citing *In re Herz*, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976) (emphasis in original)
[7] Holt, p. 10, ll. 1-9.

The presently claimed invention is directed to pharmaceutical microcapsules with enhanced taste-masking and high dissolution rate in the stomach. The invention as presently claimed encompasses microcapsules which comprise drug microparticles surrounded by a first layer consisting essentially of ethylcellulose which itself is surrounded by a second layer which comprises an acrylic polymer that is soluble in the stomach.

As discussed above, the enteric coatings of *Percel* are insoluble at the low pH levels found in the stomach, but soluble at the neutral pH levels found in the intestinal tract, and accordingly have solubility properties which are the *opposite* of the acrylic polymer coatings of the claimed invention, which are soluble in the stomach. Thus, *Percel* does not disclose, much less suggest or give motivation to use acrylic polymers that are soluble in the stomach. Since *Percel* does not suggest or teach "a second layer disposed over said first layer, comprising an acrylic polymer, wherein said acrylic polymer is soluble in the stomach, *Percel* does not render obvious the instantly claimed invention.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the §103 rejection based on Percel.

## VI. Rejection of Claims 15-24 and 26-28 under 35 U.S.C. §103(a) as being allegedly unpatentable over *Holt*.

The Examiner alleges that *Holt* teaches "a taste-masked rapid release coating system comprised of a drug core …, a spacing layer that includes ethyl cellulose and a taste-masking layer that includes Eudragit polymers.[8] Holt discloses that the materials useful for the "spacing layer" include ethyl cellulose, methyl cellulose, hydroxy propyl cellulose, hydroxy propyl methyl cellulose, polyalkylene glycols, polyalkylene oxides, sugars and sugar alcohols, waxes, shellacs, acrylics, etc. and mixtures thereof.[9] This list contains millions of possible mixtures of polymers

[8] Office Action dated 2/27/2009
[9] Holt, p. 10, ll. 1-9.

when one considers that some of the listed polymers are themselves genera of polymers (for example "polyalkylene glycols, polyalkylene oxides, sugars and sugar alcohols, waxes, shellacs, acrylics" are each a genus of polymers). All these materials, however, are not equally soluble in the stomach and do not provide instant release of a drug core in the stomach and, thus, more guidance is needed as to which spacer layer materials are useful for immediate release in the stomach. The only guidance given in Holt beyond this list is in Examples 1, 2, 3, and 4 – all of which use ethyl cellulose combined with polyvinylpyrrolidone (PVP) or hydroxy propyl methyl cellulose (HPMC). Moreover, Holt teaches that

> [r]apid release dosage forms in accordance with the present invention are those in which the drug is rapidly released from the coatings in the stomach. To the extent possible, the effect of the spacing and taste masking layers under such circumstances will be minimal in terms of reducing the normal bioavailability of the same drug if uncoated.

Given the fact that ethylcellulose is practically insoluble in water, one of skill in the art upon reading the above teaching in Holt, along with the exemplification of the disclosure of Holt, would understand that a water insoluble polymer such as ethylcellulose would need a water soluble component such as PVP and HPMC to ensure rapid release from the coatings in the stomach. The examples disclosed by Holt contain drug cores surrounded by a spacer layer that is a mixture of ethyl cellulose and either PVP or HPMC and only Examples 1 and 2 provide *both* sufficient taste-masking *and* acceptable potency and dissolution. Thus, Holt provides no motivation or teaching to remove PVP or HPMC and use ethylcellulose alone as a first layer surrounding a drug microparticle. Rather, based on the teachings of Holt, one of skill in the art would reasonably believe that when ethylcelluose is used in the spacer layer a water soluble component is needed for rapid release of the drug. Thus, the instantly claimed invention which requires the inner layer to consist essentially of ethyl cellulose is not obvious in view of Holt.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this §103 rejection.

Except for issue fees payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-1283. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. 1.136(a)(3).

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Respectfully submitted,
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